REMARKS

Applicant kindly thanks the Examiner for the opportunity to discuss the issues in this case with her during the telephone interview on January 29, 2004.

Claims 3 and 4 have been cancelled. New claims 12-23 have been added. Claims 1, 2, and 5-23 are pending. Favorable reconsideration and allowance is respectfully requested.

Information Disclosure Statement

The Applicant thanks the Examiner for noting that the listing of references in the specification on pages 22-24 is not a proper information disclosure statement. The Applicant has included all the references listed on pages 22-24 in the Information Disclosure Statement filed January 25, 2002 except for the Gennaro reference number 24. The Gennaro reference is a pharmacy text and is considered cumulative to the references submitted in the Information Disclosure Statement.

Specification

The Examiner has noted that page 3 of the Specification refers to reference "[22]" and "[23]" yet there are only 20 references listed on pages 22-23 of the Specification. The Applicant directs the Examiner to page 24 of the specification on which references 21-28 are included. A copy of page 24 is attached in the Appendix following these remarks. The Applicant respectfully asserts that references "[22]" and "[23]" are properly referred to in the Specification on page 24. The Applicant requests that the Examiner withdraw the objection to the Specification.

Claims

Claims 1 and 2 have been amended to recite that the composition comprising erythropoietin is administered to an individual at risk for developing ischemic acute renal failure prior to the individual developing ischemic acute renal failure. Support for the amendment to claims 1 and 2 may be found throughout the specification, and in particular, on page 8, lines 6-8 and lines 16-18, Example 5 on pages 16-17, and Figure

4. Claim 11 has been amended to depend from claim 8. Support for the amendment to claim 11 may be found through out the specification and on page lines 12-16. Claims 12-23 have been added. Support for claims 12 and 21 may be found on page 8, lines 8-15. Support for claims 13 and 22 may be found on page 11, lines 1-4. In addition, one of ordinary skill in the art will recognize ischemic renal failure-inducing events may include, but are not limited to, surgical events and treatment with nephrotoxic agents. Support for claims 14-20 may be found in claims 5-11. Support for claim 23 may be found in on page 11, lines 1-8 and Figure 4a. No new matter has been added.

Claim Rejections Under 35 USC §102

35 USC §102(b)

The Examiner rejected claims 1-11 under 35 USC § 102(b) as being anticipated by Westenfelder et al. (*J. Am. Soc. Nephrol.*, Sept. 2000; 11: 597A, abstract A3148). The Examiner alleges that Westenfelder et al. teach a method of treating ischemic acute renal failure by administering a composition comprising EPO and a pharmaceutically acceptable carrier. The Examiner states that Westenfelder et al. state that EPO administration ameliorated the decline in renal function (prevented any further decline in renal function) and accelerated functional recovery and that EPO acts as a mitogen and motogen for renal tubular cells. The EPO administered was contained in a pharmaceutically acceptable diluent and was administered systemically at 300 U/kg, 2-4 times, 24 hours apart.

The Applicant respectfully asserts that the subject matter of newly amended independent claims 1 and 2 is not taught by the Westenfelder et al. abstract. The Westenfelder et al. abstract discusses that "EPO-deficiency" induced during ARF may contribute to the severity of ischemic ARF because it may represent a state of "growth factor withdrawal". The Westenfelder et al. abstract teaches "replacement" of EPO in rats that already have ischemic acute renal failure.

In contrast, the Applicant's newly amended claims 1 and 2 recite a method of preventing or treating, respectively, ischemic acute renal failure in an individual **at risk** for developing ischemic acute renal failure by administering a composition comprising

EPO **prior to** the individual developing ischemic acute renal failure. As described in the specification, "In patients at risk for developing ischemic ARF, such as patients entering surgery, the preferred treatment protocol includes administering a dose of between 250-350 U/kg body weight of EPO in a pharmacological composition up to six hours prior to the ischemic ARF-inducing event." (Page 11, lines 1-4.) In addition, the Applicant discusses the benefits of preventing ischemic ARF stating, "Prevention of ischemic ARF will lead to a very substantial cost savings, since the need for acute hemodialysis would be eliminated or reduced, and the many complications of ischemic ARF (uremic bleeding, hyperkalemia, acidosis, pericarditis, arrhythmias, neurological complications) and those of hemodialysis per se would be ameliorated or avoided. (Page 12, lines 3-8.) The Applicant identifies a group of individuals who are at risk for developing ARF, including, but not limited to, patients with diabetes mellitus, patients with underlying renal insufficiency or with nephritic syndrome, old age, patients with atherosclerotic disease, patients who are given nephrotoxic agents (radio contrast media, aminoglycosides, cis-platinum, cyclosporine A, FK506) or patients who are septic, hypotensive, hypoxic, who undergo surgery (aortic aneurysm, cardiac repair), or who have myoglobinuria-hematuria, pregnancy associated ARF, or significant liver disease. (Page 8, lines 8-15.)

The Westenfelder et al. abstract fails to teach a method of preventing or treating ischemic acute renal failure in an individual **at risk** for developing ischemic acute renal failure by administering a composition comprising EPO **prior to** the individual developing ischemic acute renal failure as claimed in newly amended claims 1 and 2.

Thus, the Applicant asserts that the claimed invention is not anticipated by Westenfelder et al. Applicants respectfully request the rejection of claims 1, 2, and 5-11 as being anticipated by Westenfelder et al. under 35 USC §102(b) be withdrawn.

The Examiner rejected claims 1-6 under 35 USC §102(b) as being anticipated by Nemoto et al. (*J. Am. Soc. Nephrol.*, Sept. 2000; 11: 594A, abstract A3134). The Examiner states that Nemoto et al. teach a method of preventing and treating ischemic acute renal failure by administering a composition comprising EPO and a pharmaceutically acceptable carrier. The Examiner notes that with respect to present claims 1 and 3, "preventing" is treated here as meaning treating so as to delay or

ameliorate acute renal failure (e.g. preventing further decline in renal function). Nemoto et al. allegedly teach that there was a systemic response to the administration of EPO and that EPO treatment led to an increase in hematocrit. The Examiner states that prevention of cell apoptosis in renal tubular cells and stimulation of motogenesis and mitogenesis in renal tubular cells are inherent properties of EPO that would have occurred after administration of EPO.

The Applicant respectfully traverses the Examiner's rejection based on Nemoto et al. Applicants respectfully request reconsideration of the rejected claims in light of the amended claims and the traversals discussed below.

Nemoto et al. teach EPO treatment **during** ARF. EPO was administered to rats having ARF at 500 or 3000 units/kg. The EPO treatment led to a rapid and significant increase in hematocrit at 48 and 72 hours after moderate ischemic renal reperfusion injury. Higher dose (3000 units/kg) EPO led to a more pronounced increase in hematocrit in sever ischemic renal reperfusion injury.

In contrast, as described above, the Applicant's claimed invention recites a method of preventing and a method of treating individuals at risk for developing ischemic acute renal failure by administering a composition comprising EPO **prior to** the individual developing ischemic acute renal failure as claimed in newly amended claims 1 and 2. Nemoto et al. fail to teach the Applicant's claimed invention in the abstract describing EPO given to rats already having ARF.

Thus, the Applicant asserts that the claimed invention is not anticipated by Nemoto et al. The Applicant respectfully requests the rejection of claims 1-2 and 5-6 under 35 USC §102(b) be withdrawn.

35 USC §102(a)

The Examiner rejected claims 1-6 under 35 USC §102(a) as being anticipated by Westenfelder et al. (*J. Am. Soc. Nephrol.*, Sept. 2001; 12:739A).

The Applicant has filed a Katz Declaration under 37 CFR §1.132 stating that this reference is the Applicant's own publication.

Therefore, the Applicant respectfully requests that the rejection of claims 1-2 and 4-6 under 35 USC §102(a) be withdrawn.

The Examiner rejected claims 1-6 under 35 USC §102(a) as being anticipated by Westenfelder et al. (*J. Invest. Med.*, January 2001, 49(1): 59A, abstract 319).

The Applicant has filed a Katz Declaration under 37 CFR §1.132 stating that this reference is the Applicant's own publication.

Therefore, the Applicant respectfully requests that the rejection of claims 1-2 and 5-6 under 35 USC §102(a) be withdrawn.

The Examiner has rejected claims 2-7 under 35 USC §102(a) as being anticipated by Nemoto et al. (*Kidney Intl.*, January 2001, 59: 246-251). The Examiner alleges that Nemoto et al. teach a method of treating ischemic acute renal failure by systemic administration of a therapeutically effective amount of recombinant erythropoietin and a pharmaceutically acceptable carrier. The Examiner alleges that Nemoto et al. state that EPO may change the course of tubular repair. The Examiner states that prevention of harmful cell apoptosis in renal tubular cells and stimulation of motogenesis and mitogenesis in renal tubular cells in an inherent activity of EPO and woiud have occurred upon administration of EPO.

The Applicant respectfully traverses the Examiner's rejection of claims 2-7 as being anticipated by Nemoto et al. Nemoto et al. teach that recombinant EPO can rapidly increase the hematocrit and improve mortality **during** ARF. (Conclusions, p. 246.) Nemoto et al. teach away from Applicant's claimed invention, stating, "EPO treatment during moderate or severe renal IRI did not change the course of the renal dysfunction." (Results, p. 246Nemoto et al. induced ischemic ARF in rats and during ARF, EPO was administered in doses of 500 U/kg and 3000 U/kg.

As discussed above, the Applicant's claimed invention recites a method of preventing and a method of treating individuals at risk for developing ischemic acute renal failure by administering a composition comprising EPO **prior to** the individual developing ischemic acute renal failure as claimed in newly amended claims 1 and 2. As described in the specification, "prophylactic administration of EPO, followed by daily injections, both ameliorated the loss in renal function (as assessed by serum creatinine levels) and accelerated functional recovery. (Page 16, lines 20-22, Figure 4.) Nemoto et al. reference fails to teach a method of preventing or treating ischemic acute renal failure in an individual **at risk** for developing ischemic acute renal failure by

administering a composition comprising EPO **prior to** the individual developing ischemic acute renal failure as claimed in newly amended claims 1 and 2.

Thus, the Applicant asserts that the claimed invention is not anticipated by Nemoto et al. The Applicant respectfully requests the rejection of claims 2 and 5-7 under 35 USC §102(a) be withdrawn.

SUMMARY

Pending Claims 1-2 and 5-11 as amended are patentable. New claims 12-23 are also patentable. Applicant respectfully requests the Examiner grant early allowance of this application. The Examiner is invited to contact the undersigned attorneys for the Applicant via telephone if such communication would expedite this application.

Respectfully submitted,

Heidi A. Dare

Heidi A. Dare
Registration No. 50,775
Attorney for Applicant

BRINKS HOFER GILSON & LIONE
P.O. BOX 10395
CHICAGO, ILLINOIS 60610
(312) 321-4200

APPENDIX

Our Case No. 10402/15
U-3253

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Application of:

Christof Westenfelder

Serial No. 10/003,352

Filing Date: November 1, 2001

For METHOD OF USE OF ERYTHROPOEITIN

Examiner Holly Schnizer

Group Art Unit No. 1653

KATZ DECLARATION

Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

SIR:

I, Christof Westenfelder, hereby declare and state that:

1. I am the inventor of the subject matter described and claimed in U.S. Patent Application Serial Number 10/003,352, filed November 1, 2001, entitled METHOD OF USE OF ERYTHROPOEITIN.

2. I am the co-author of the following publications, Erythropoietin (EPO) Treatment Ameliorates Ischemic Acute Renal Failure (ARF) in Rats by Its Anti-Apoptotic, Motogenic and Mitogenic Actions, *J. Am. Soc. Nephrol.*, September, 2001, Vol. 12, p. 739A, Abstract A3857, and Anti-Apoptotic, Mitogenic, and Motogenic Actions of Erythropoietin on Tubular Cells Protect Renal Function and Accelerate Recovery form Ischemic Acute Renal Failure in Rats, *J. Invest. Med.*, January, 2001, Vol. 49, No. 1, p. 89A, Abstract 319 (hereinafter the publications").

3. I am the sole inventor of the subject matter common to both the above-

identified U.S. Patent Application and the publications.

4. The other authors of the publications, Robert L Baranowski and FG Toback, were working under my direction.

5. While co-authors of the publications, Robert L Baranowski and FG Toback made no inventive contribution to the subject matter claimed in U.S. Patent Application Serial Number 10/003,352, and therefore, are not co-inventors of the subject matter claimed in U.S. Patent Application Serial Number 10/003,352.

6. The undersigned petitioner declares further that all statements made herein of his own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code and that such willful false statements may jeopardize the validity of this application or any patent issuing thereon.

7. Further declarant saith not.

02/03/2004
Date

Christof Westenfelder
Christof Westenfelder

21. Westenfelder C et al.: Human, rat and mouse kidney cells express functional erythropoietin receptors. *Kidney Int* 55:808-820, 1999

22. Vaziri N et al.: Erythropoietin enhances recovery from cisplatin-induced acute renal failure. *Am J Physiol* 266:F360-F366, 1994

23. Nemoto T et al.: Recombinant erythropoietin rapidly treats anemia in ischemic acute renal failure. *Kid. Int* 59:246-251, 2001

24. Gennaro AR: The science and practice of pharmacy. Lippincott, Williams & Wilkins, Philadelphia, PA

25. Lieberthal W et al.: Necrosis and apoptosis in acute renal failure. *Semin Nephrol* 18:505-518, 1998

26. Kartha S, Toback FG: Adenine nucleotides stimulate migration in wounded cultures of kidney epithelial cells. *J Clin Invest* 90:288-292, 1992

27. Westenfelder C et al.: Renal tubular function in glycerol-induced acute renal failure. *Kidney Int* 18:432-444, 1980

28. McWhinnie DL et al.: Morphometric analysis of cellular infiltration assessed by monoclonal antibody labeling in sequential human renal allograft biopsies. *Transplantation* 42:352-358, 1986